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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,090	03/11/2004	Ivan Richards	04-183 (400.147)	6030

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EXAMINER	
BOWMAN, AMY HUDSON	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/798,090	RICHARDS ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,10-21,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,10-21,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 11/8/2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 8/8/2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 2, 4-9 and 22-29 have been cancelled. Claims 1, 3, 10-21, 30 and 31 are pending in the application.

Response to Priority

As stated in the office action mailed 8/8/2005, applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

In the instant case, the effective filing date of the instant claims is determined to be that of the instant application 10/798,090, which has an effective filing date of 3/11/2004. The instant case 10/798,090 does not receive the benefit of any of the earlier filed priority documents because the instantly recited target, CHRM3, is not disclosed in the specification or claims of the priority applications. Thus, the instant application 10/798,090 is accorded an effective filing date of 3/11/2004.

Applicant argues that the present application claims priority to 60/363,124 filed March 11, 2002 and points to support for the instant claim limitations in 60/363,124.

Applicant's argument has been considered but is not found persuasive. The priority provisional filed on March 11, 2002 expires within one year. There are no documents that arose from 60/363,124 for which priority is being claimed that recite the instantly claimed target, CHRM3. The intervening references do not recite the instant target and therefore the instant application does not receive benefit of 60/363,124.

Response to Arguments--Claim Rejections - 35 USC § 103(a)

Claims 1, 3, 10-21, 30 and 31 stand rejected under 35 U.S.C. 103(a), as being unpatentable over Elbashir et al., in view of Forsythe et al., Sato et al., Tuschl et al. (WO 02/44321), Matulic-Adamic et al. (U.S. 5,998,203), and Morrissey et al. (US 2003/0206887), for the reasons of record set forth in the office action mailed 8/8/2005. Applicant has cancelled claims 2, 4-9 and 22-29, obviating the rejection against these claims.

Applicant argues that Morrissey et al. (US 2003/0206887 A1) is not prior art to the instant application and cannot be considered in this rejection. Contrary to applicant's assertion, Morrissey et al. does constitute prior art under based on the filing date of September 16, 2002, for the reasons explained in the "Response to Priority" section above. Applicant argues that Elbashir and Tuschl teach siRNA technology generally, but fail to teach, mention, or suggest siNAs targeting CHRM3 RNA comprising SEQ ID NO: 305. The examiner did not rely on Elbashir or Tuschl for teachings regarding CHRM3 RNA. Elbashir and Tuschl were relied upon for teachings of RNAi and common modifications to siRNA duplexes, therefore rendering such modifications obvious. Applicant argues that neither Forsythe et al. or Sato et al. cure the deficiencies of Elbashir and Tuschl because they do not teach double stranded nucleic acid molecules targeting CHRM2 RNA comprising SEQ ID NO: 305. The examiner did not rely on Forsythe et al. or Sato et al. for such teachings, but rather relied on Forsythe et al. for teaching the cDNA sequence encoding the human m3 muscarinic receptor gene, which corresponds to instant SEQ ID NO: 305 and relied on Sato et al. for teaching that muscarinic receptor agonists modulate the functions of lymphocytes and that the quantity of such receptors on lymphocytes is associated with the etiology of some neurological diseases such as Alzheimer's and Parkinson's diseases, thus suggesting that modulating the expression of this gene would be beneficial. As taught by Elbashir et al. and Tuschl et al., siRNA molecules are beneficial means of inhibiting target gene expression of a gene with a known sequence. Finally, applicant argues that Matulic-Adamic et al. is not art that the ordinary artisan would

consider in making the claimed invention and states that it is non-analogous art. Contrary to applicant's assertion, ribozymes are in the field of sequence specific mediators of target gene expression and share many of the same chemical modifications as antisense oligonucleotides and siRNA molecules. Applicant argues that Matulic-Adamic is simply not pertinent to the problem addressed by the presently claimed compounds, which is to provide new molecules having utility for cleaving CHRM3 target RNA by an RNAi mechanism. Applicant's argument has been considered but is not found persuasive in view of the instant claims and specification.

As explained in the office action mailed on 8/8/2005, the instant specification defines the term "siNA" on page 69, to refer to **any nucleic acid molecule** capable of inhibiting or down regulating gene expression or viral replication, **for example** by mediating RNAi or gene silencing in a sequence-specific manner. Ribozymes are capable of inhibiting gene expression by mediating cleavage in a sequence-specific manner, falling within the scope of "for example by mediating RNAi or gene silencing in a sequence-specific manner". Furthermore, the teachings of Matulic-Adamic et al. meet the limitations of the instant claims, comprising a sense and an antisense strand wherein each strand is about 18 to about 27 nucleotides in length. Matulic-Adamic et al. was not relied upon for specificity to CHRM3, but is relied upon for teaching an inhibitory nucleic acid molecule meeting the instant limitations of the term "siNA" that comprises modifications and linkers that were known to add specific benefits to oligonucleotides at the time the invention was made. Additionally, the ribozymes are taught to be targeted to virtually any RNA transcript and achieve efficient cleavage (see

column 1) and to be sufficiently complementary to a target sequence to allow cleavage. Additionally, the specification does not disclose a definition for RNAi that excludes the enzymatic molecules taught by Matulic-Adamic et al. The instant specification discloses on page 72 that "as used herein, the term RNAi is meant to be equivalent to other terms used to describe sequence specific RNA interference, such as post transcriptional gene silencing, translational inhibition, or epigenetics." Ribozymes are known molecular tools for specific inhibition of gene translation and interfere with RNA. However, regardless of the interpretation of ribozymes as "siNA" molecules, the teachings of Matulic-Adamic et al. are relied upon for modifications and linkers that were known and commonly utilized in the oligonucleotide art and not for specifically targeting CHRM3 through the specific mechanism being instantly argued. Applicant asserts that they are unaware of a single instance in which a teaching regarding ribozymes has provided any insight into RNAi. Contrary to applicant's assertion, ribozymes and siRNA are accepted in the field as sequence specific mediators of inhibition of target gene expression and are each commonly modified in the same manner to increase efficiency of delivery in the cell. For example, Escobedo et al. (WO 02/096927), which has a common inventor with the instant application (McSwiggen), teaches that siRNA and ribozymes are utilized to target and inhibit the expression of VEGF and VEGFr genes (see for example, page 6) and teaches common chemical modifications to each. Contrary to applicant's assertion that "a mere identification of a target (Sato) and a general mechanism for suppressing expression (Elbashir and Tuschl) without more is not the type of particularized suggestion necessary to sustain an obviousness rejection", Sato does not merely

identify target, but clearly establishes a motivation to inhibit the target, as explained above. Elbashir and Tuschl teach a commonly utilized tool of inhibiting target genes, siRNAs. Applicant further argues that there is no reasonable expectation of success. Applicant's assertion that there is not reasonable expectation of success seems to depend on the assertion that the priority date of the instant application is at least March 11, 2002. Contrary to applicant's assertion, the instant claims are accorded an effective filing date of 3/11/2004, for the reasons explained in the "Response to Priority" section above. Applicant further asserts that one of ordinary skill in the art, as of 3/11/2002 would not have had a reasonable expectation of success based on the teachings relied upon by the examiner. Applicant asserts that in absence of a teaching of a double stranded nucleic acid molecule as presently claimed, one skilled in the art would have no reasonable expectation of success of making such a molecule. Contrary to applicant's assertions, Sato et al. offers motivation to inhibit human CHRM3, as explained above and Elbashir and Tuschl et al. offered a reasonable expectation of success to target and inhibit a known gene sequence with a siRNA at the time the invention was made.

Response to Arguments—Double Patenting

Claims 1, 3, 10-21, 30 and 31 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending application 10/919,866 for the reasons of record set forth in the

office action mailed 8/8/2005. Applicant has cancelled claims 2, 4-9 and 22-29, obviating the rejection against these claims.

Applicant has requested to defer addressing this rejection until the claims are otherwise in condition for allowance.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is 571-272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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Amy H. Bowman
Examiner
Art Unit 1635

J.D. SCHULTZ, Ph.D.
PATENT EXAMINER